

- d) contacting the gp160 with an alkylating agent;
- e) contacting the gp160 with an oxidizing agent;
- f) contacting the gp160 with an ionic detergent, and
- g) dialyzing the gp160 against a neutral detergent.

19. (Amended) A method of producing the trimer according to any one of claims 11- 12, the method comprising, in order:

- a) expressing gp160;
- a) purifying the gp160;
- b) contacting the gp160 with an ionic detergent;
- c) contacting the gp160 with a reducing agent;
- d) contacting the gp160 with an oxidizing agent; and
- e) dialyzing the gp160 against a neutral detergent.

*BB*  
Please add new claims 20-31.

*Sub. C1*  
*B7*  
20. (New) A method of producing the trimer according to claim 13, the method comprising, in order:

- a) expressing gp160 having its transmembrane region deleted therefrom;
- b) purifying the gp160;
- c) contacting the gp160 with a reducing agent;
- d) contacting the gp160 with an alkylating agent;
- e) contacting the gp160 with an oxidizing agent;
- f) contacting the gp160 with an ionic detergent, and
- g) dialyzing the gp160 against a neutral detergent.

21. (New) A method of producing the trimer according to any one of claims 13, the method comprising, in order:

- a) expressing gp160 having its transmembrane region deleted therefrom;
- b) purifying the gp160;
- c) contacting the gp160 with an ionic detergent;
- d) contacting the gp160 with a reducing agent;
- e) contacting the gp160 with an oxidizing agent; and
- f) dialyzing the gp160 against a neutral detergent.

22. (New) A composition comprising a purified trimer of HIV gp160 comprising a gp41 fragment essential for trimer formation and an immunogenic fragment of gp120, wherein the trimer:
- binds to CD4;
  - binds to an anti-gp120 antibody capable of neutralizing HIV infection of cells *in vitro*;
  - binds to an anti-gp41 antibody; and
  - has no inter-chain disulfide bridges.
23. (New) The composition according to claim 22, wherein the gp41 and gp120 are from different HIV strains.
24. (New) The composition according to any one of claims 22 - 23 having a protein content that comprises more than 50% of the trimer.
25. (New) The composition according to any one of claims 22 - 23 wherein the binding affinity of the trimer to CD4 is equal or greater than the binding affinity of gp120 of an infectious HIV.
26. (New) The composition of any one of claims 22 - 23 further comprising an adjuvant.
27. (New) The composition according to claim 26 wherein the trimer is the only HIV surface antigen in the composition.
28. (New) A method of producing the trimer according to any one of claims 22 - 23, the method comprising, in order:
- expressing a gp160 fragment comprising gp41 and an immunogenic gp120 fragment;
  - purifying the gp160 fragment;
  - contacting the gp160 fragment with a reducing agent;
  - contacting the gp160 fragment with an alkylating agent;
  - contacting the gp160 fragment with an oxidizing agent;
  - contacting the gp160 fragment with an ionic detergent, and
  - dialyzing the gp160 fragment against a neutral detergent.
29. (New) A method of producing the trimer according to any one of claims 22- 23, the method comprising, in order:
- expressing a gp160 fragment comprising gp41 and an immunogenic gp120 fragment;

- b) purifying the gp160 fragment;  
c) contacting the gp160 fragment with an ionic detergent;  
d) contacting the gp160 fragment with a reducing agent;  
e) contacting the gp160 fragment with an oxidizing agent; and  
f) dialyzing the gp160 fragment against a neutral detergent.

30. (New) The composition according to claim 22 wherein the gp41 fragment essential for trimer formation comprises gp41 lacking its transmembrane domain.

31. (New) The composition according to claim 30 wherein the gp41 fragment comprises the 129 N-terminal amino acids of gp41.

#### REMARKS

The specification has been amended to recite the priority claim in the first line of the specification and to add an abstract. The abstract is substantively the same as appearing in the parent PCT application and, therefore, does not introduce new matter. The specification has also been amended to add a brief description of the drawing. The description is substantively the same as appearing in Example 1 of the specification and, therefore, does not introduce new matter.

#### Rejection of claims 11-19 under 35 U.S.C. § 112, first paragraph

The claims were rejected for failing to meet the written description requirement, the Office Action alleging that the claims purported to encompass a gp160 trimer lacking interchain disulfide linkages that was naturally occurring whereas naturally occurring gp160 trimers were, by contrast, known to contain interchain disulfide linkages. The applicants respectfully traverse. In fact, naturally occurring trimers are known **not** to contain inter-chain disulfide linkages. Nevertheless, the rejection is rendered moot by the foregoing amendments, which delete "naturally occurring" and "recombinant" from the claims. The claims now simply recite a gp160 trimer with no limitation as to the source of the gp160 monomers comprising the trimer (i.e., the monomers may come from a naturally occurring or recombinant source).

Claims 18 and 19 were further rejected for lacking enablement for gp160 fragments other than gp160 having the transmembrane region deleted therefrom. The amendments to claims 18 and 19 obviate this rejection. However, new claims 22-31 are specifically directed to trimers comprising both gp41 fragments and gp160 fragments.